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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/774,181	04/26/2001	Bernhard A. Sabel	202306US0PCT	8612

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EXAMINER

OH, SIMON J

ART UNIT PAPER NUMBER

1615

DATE MAILED: 08/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/774,181

Applicant(s)

SABEL ET AL.

Examiner

Simon J. Oh

Art Unit

1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11 and 15-34 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 11 and 15-34 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____. | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

Claim Objections

1. Claim 29 objected to because of the following informalities: There is a period missing from the end of the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 27 contains the trademarks/trade names GENAPOL™ and BAUKIT™. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a stabilizer/surfactant and, accordingly, the identification/description is indefinite.

Art Unit: 1615

3. Regarding Claim 28, the word “as” renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

4. Claims 11, 15-24, and 26-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Kreuter *et al.* (WIPO Document No. WO 95/22963)

The Kreuter *et al.* document discloses a nanoparticle composition that allows the delivery of drugs across the blood-brain barrier. The composition comprises a polymeric material and a drug that is absorbed, adsorbed, or incorporated within the nanoparticles themselves. The nanoparticles are also coated with at least one surfactant, which allows for the delivery of drugs across the blood-brain barrier. Suitable carriers for the nanoparticles include buffers or other physiologically acceptable carrier solution. The nanoparticles possess a diameter ranging from 1 nm to 1,000 nm, and may be delivered orally, intravenously, or intramuscularly to mammals,

Art Unit: 1615

including humans. The drugs that may be used with the nanoparticle composition include those substances that affect or act on the nervous system, including tumor tissue. Such substances that may be used include diagnostic agents (See Summary of the Invention, Pages 6-7; and Page 11, 2nd Paragraph). More specific examples of suitable drugs include chemotherapeutic agents; anti-cancer drugs; and hormones and hormone antagonists (See Page 11, 4th Paragraph). Specific types of anti-cancer drugs listed include alkylating agents, antimetabolites, nitrogen mustards, ethylenamines, methylmelamines, alkylsulfonates, folic acid analogs, pyrimidine analogs, purine analogs, vinca alkaloids, and antibiotics (See Page 13, Lines 8-10). Specific types of polymers suitable for use in the composition include polyacetates, polystyrenes, polyvinyls, polyacrolein, gelatin, albumin, polysaccharides, and polyglutaraldehyde (See Page 9, 2nd Paragraph). Specific types of surfactants suitable for use in the composition include polaxamers, polysorbates, sodium lauryl sulfate, metal salts of fatty acids, metal salts of fatty alcohol sulfates, ethoxylated phenols, ethoxylated diphenols, ethoxylated triglycerides, glycerol monostearate and surfactants of the Genapol™ and Bauki™ series (See Page 10). The use of dextran 70,000 as a stabilizer is disclosed (See Pages 14-15, Examples 1 and 2).

5. Claims 11, 15-24, and 26-34 are rejected under 35 U.S.C. 102(e) as being anticipated by Sabel *et al.* (WIPO Document No. WO 98/56361)

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the

Art Unit: 1615

inventor of this application and is thus not the invention “by another,” or by an appropriate showing under 37 CFR 1.131.

The Sabel *et al.* document discloses a nanoparticle composition that allows the delivery of drugs across the blood-brain barrier. The composition comprises a polymeric material; a drug that is adsorbed or incorporated within the nanoparticles; and at least one stabilizer, which allows for the delivery of drugs across the blood-brain barrier (See Summary of the Invention, Pages 5-9). Suitable carriers for the nanoparticles include water and physiologically acceptable carrier solutions containing salts and/or buffers (See Page 17, 2nd Paragraph; and Page 20, Line 23 to Page 21, Line 7). The nanoparticles possess a diameter ranging from 1 nm to 1,000 nm (See Page 11, Lines 1-2), and may be delivered orally, intravenously, or intramuscularly to mammals, including humans (See Page 22, Line 21 to Page 23, Line 12). The drugs that may be used with the nanoparticle composition include those substances that affect or act on the nervous system, including tumor tissue (See Page 12, middle paragraph). More specific examples of suitable drugs include chemotherapeutic agents; anti-cancer drugs; and hormones and hormone antagonists (See Page 13). Specific types of anti-cancer drugs listed include alkylating agents, antimetabolites, nitrogen mustards, ethylenamines, methylmelamines, alkylsulfonates, folic acid analogs, pyrimidine analogs, purine analogs, vinca alkaloids, and antibiotics (See Page 15, Lines 1-3). Specific types of polymers suitable for use in the composition include polystyrenes, polyacrylates, polyvinyls, polyacrolein, polyglutaraldehyde, polysaccharides, gelatin, and albumin (See Page 18, Lines 1-6). Specific types of stabilizers suitable for use in the composition include polaxamers, polysorbates, sodium stearate, sodium lauryl sulfate, metal salts of fatty acids, metal salts of fatty alcohol sulfates, ethoxylated phenols, ethoxylated diphenols,

Art Unit: 1615

ethoxylated triglycerides, glycerol monostearate and surfactants of the Genapol™ and Bauki™ series. Specific surfactants disclosed include polysorbate 85, polysorbate 81, and dextran 12,000 (See Page 16, 3rd Paragraph). See also Pages 27-35, Claims 1-5, 7, 9, 11-16, 18, 20, 22, 23, 27, 29-33, and 36-40.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 11 and 15-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kreuter *et al.* in view of Sabel *et al.* and Stainmesse *et al.* (U.S. Patent No. 5,133,908)

The Kreuter *et al.* document discloses a nanoparticle composition that allows the delivery of drugs across the blood-brain barrier. The composition comprises a polymeric material and a drug that is absorbed, adsorbed, or incorporated within the nanoparticles themselves. The nanoparticles are also coated with at least one surfactant, which allows for the delivery of drugs across the blood-brain barrier. Suitable carriers for the nanoparticles include buffers or other physiologically acceptable carrier solution. The nanoparticles possess a diameter ranging from 1 nm to 1,000 nm, and may be delivered orally, intravenously, or intramuscularly to mammals, including humans. The drugs that may be used with the nanoparticle composition include those substances that affect or act on the nervous system, including tumor tissue. Such substances that may be used include diagnostic agents (See Summary of the Invention, Pages 6-7; and Page 11,

Art Unit: 1615

2nd Paragraph). More specific examples of suitable drugs include chemotherapeutic agents; anti-cancer drugs; and hormones and hormone antagonists (See Page 11, 4th Paragraph). Specific types of anti-cancer drugs listed include alkylating agents, antimetabolites, nitrogen mustards, ethylenamines, methylmelamines, alkylsulfonates, folic acid analogs, pyrimidine analogs, purine analogs, vinca alkaloids, and antibiotics (See Page 13, Lines 8-10). Specific types of polymers suitable for use in the composition include polyacetates, polystyrenes, polyvinyls, polyacrolein, gelatin, albumin, polysaccharides, and polyglutaraldehyde (See Page 9, 2nd Paragraph). Specific types of surfactants suitable for use in the composition include polaxamers, polysorbates, sodium lauryl sulfate, metal salts of fatty acids, metal salts of fatty alcohol sulfates, ethoxylated phenols, ethoxylated diphenols, ethoxylated triglycerides, glycerol monostearate and surfactants of the Genapol™ and Bauki™ series (See Page 10). The use of dextran 70,000 as a stabilizer is disclosed (See Pages 14-15, Examples 1 and 2).

The Sabel *et al.* document discloses a nanoparticle composition that allows the delivery of drugs across the blood-brain barrier. The composition comprises a polymeric material; a drug that is adsorbed or incorporated within the nanoparticles; and at least one stabilizer, which allows for the delivery of drugs across the blood-brain barrier (See Summary of the Invention, Pages 5-9). Suitable carriers for the nanoparticles include water and physiologically acceptable carrier solutions containing salts and/or buffers (See Page 17, 2nd Paragraph; and Page 20, Line 23 to Page 21, Line 7). The nanoparticles possess a diameter ranging from 1 nm to 1,000 nm (See Page 11, Lines 1-2), and may be delivered orally, intravenously, or intramuscularly to mammals, including humans (See Page 22, Line 21 to Page 23, Line 12). The drugs that may be used with the nanoparticle composition include those substances that affect or act on the nervous system,

Art Unit: 1615

including tumor tissue (See Page 12, middle paragraph). More specific examples of suitable drugs include chemotherapeutic agents; anti-cancer drugs; and hormones and hormone antagonists (See Page 13). Specific types of anti-cancer drugs listed include alkylating agents, antimetabolites, nitrogen mustards, ethylenamines, methylmelamines, alkylsulfonates, folic acid analogs, pyrimidine analogs, purine analogs, vinca alkaloids, and antibiotics (See Page 15, Lines 1-3). Specific types of polymers suitable for use in the composition include polystyrenes, polyacrylates, polyvinyls, polyacrolein, polyglutaraldehyde, polysaccharides, gelatin, and albumin (See Page 18, Lines 1-6). Specific types of stabilizers suitable for use in the composition include polaxamers, polysorbates, sodium stearate, sodium lauryl sulfate, metal salts of fatty acids, metal salts of fatty alcohol sulfates, ethoxylated phenols, ethoxylated diphenols, ethoxylated triglycerides, glycerol monostearate and surfactants of the Genapol™ and Bauki™ series. Specific surfactants disclosed include polysorbate 85, polysorbate 81, and dextran 12,000 (See Page 16, 3rd Paragraph).

Neither the Kreuter *et al.* nor the Sabel *et al.* document discloses of a nanoparticle composition comprising doxorubicin or mitoxantrone as a drug.

The Stainmesse *et al.* patent teaches a nanoparticle formulation and a method for its preparation (See Abstract). The nanoparticles are preferably less than 500 nm in diameter and an active substance in a polymer matrix. The examples of suitable polymer material include gelatin, polylactic acid, and copolymers of acrylic acid, acrylates, and acrylic acid polymers (See Column 2, Line 27 to Column 3, Line 45). Examples are given where nanoparticles comprising doxorubicin as the drug and Polaxamer 188 as the surfactant (See Column 5-7, Examples 1, 6, and 7). A process of preparing a suspension of the nanoparticles in a solution sodium chloride is

Art Unit: 1615

disclosed, as well as the administration of such nanoparticles by intravascular injection (See Column 9, Line 41 to Column 10, Line 8).

It would be obvious to one of ordinary skill in the art to combine the teachings of Kreuter I, Sabel *et al.*, and Stainmesse *et al.* into the objects of the instant application. One of ordinary skill would be motivated to do so, because as stated in *In re Kerkhoven*, 205 USPQ 1069, 1072 (CCPA- 1980), “It is prima facie obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose.” As this court explained in *Crockett*, 126 USPQ 186, 188 (CCPA- 1960), the idea of combining them flows logically from their having been individually taught in the prior art. In the instant case, all three references teach nanoparticle compositions that comprise a polymer material, a drug, and a stabilizer or surfactant. Regarding the claim limitations drawn to a method treating cancer, and more particularly brain cancer, the critical feature of the inventions disclosed in Kreuter I and Sabel *et al.* of the delivery of a drug across the blood-brain barrier, along with the disclosure of the use of anti-cancer drugs in the nanoparticle composition makes such treatment methods obvious to one of ordinary skill in the art. Thus, the claimed invention as a whole is *prima facie* obvious.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Simon J. Oh whose telephone number is (703) 305-3265. The examiner can normally be reached on M-F 8:30 am to 5:00 pm.


Art Unit: 1615

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (703) 308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Simon J. Oh
Patent Examiner
AU 1615

sjo
August 6, 2002


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